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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,034	12/14/2004	Garfield P. Royer	1729-33	5418

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,034	ROYER, GARFIELD P.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 19-41* is/are pending in the application.

4a) Of the above claim(s) *7,9,10,20,21,23,27,30,31 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,11,12,19,22,24-26,28,29,32-34 and 36-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response after Non-Final Office Action and Applicant's Arguments/Remarks, all filed 03/13/09 is acknowledged.

Applicant has overcome the following rejections by virtue of persuasive remarks: The non-statutory double patenting rejections over the (1) 6,869,976 Patent; 6,391,336 Patent; and 6,497,901 Patent and the provisional double patenting rejection over copending Application No. 10/838,303 have been withdrawn.

Claims 1-6, 8, 11, 12, 19, 22, 24-26, 28-29, 32-34 and 36-41 are being examined in this action. No amendments to the claims have been made herein. Claims 13-18 and 42-68 have previously been cancelled. Claims 7, 9, 10, 20, 21, 23, 27, 30, 31 and 35 have been withdrawn (non-elected invention). Claims 1-6, 8, 11, 12, 19, 22, 24-26, 28-29, 32-34 and 36-41 remain rejected.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-6, 8, 11, 12, 19, 22, 24-26, 28-29, 32-34 and 36-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito *et al.* (hereinafter "Saito") (U.S. Patent No. 6,344,209) in view of Bell *et al.* (hereinafter "Bell") (U.S. Pat. Appln. Publn. No. 2002/0055143 A1).

Saito ('209) teaches an apatite-coated solid composition containing a biodegradable polymer; an apatite-coated solid composition containing a biodegradable polymer and a medicinal substance having sustained release properties and a method for producing the solid composition (see column 1, lines 6-10); (col. 2, line 39 – col. 3, line 37) and Abstract.

Suitable biodegradable polymers disclosed include hyaluronates, polyethylene glycol and gelatin, for example (col. 4, lines 43-64).

Suitable medicinal substances disclosed are anti–tumor agents including antineoplastic agents such as cisplatin (col. 6, line 65 – col. 7, line 3). The medicinal substance is employed before molding with the aid of suitable excipients such as calcium sulfate hemihydrate (col. 15, lines 21-33).

The pharmaceutical composition can be produced by dissolving a biodegradable polymer in which the medicinal substance is dispersed and forming the solution into spheres, rods, needles, pellets, films or the like by an appropriate method (col. 17, lines 59-67).

In accordance with the invention, a substrate, i.e., (1) a solid composition containing a biodegradable polymer, (2) a solid composition containing a biodegradable polymer and a medicinal substance is immersed in an apatite-forming buffer solution so as to coat the surface of the substrate with apatite. The substrate is preferably used in granular form (granules, fine particles, fine granules) (col. 15, lines 8-20); (col. 16, lines 1-9).

The apatite-coated solid composition can be processed into an injectable product by suspending the composition together with a dispersant, using for example, polysaccharides such as hyaluronic acid (col. 20, lines 9-32).

The apatite-coated solid composition can be used to treat and repair bone tissue after surgery for lung cancer, breast cancer, etc. (col. 20, lines 43-58).

The examples at columns 22-24 demonstrate processes for preparing the apatite-coated solid compositions which contain biodegradable polymers.

Saito does not teach an immunostimulant such as GM-CSF.

Bell ('143) teaches bone precursor compositions suitable for injection, which contain calcium sulfate hemihydrate, therapeutic agents and colony stimulating factors (CSF), such as GM-CSF. The colony stimulating factors (growth factors) are beneficial in the regulation of differentiation and development. See ¶s [0009-0010]; [0056]; [0069]. Additional agents disclosed include chondroitin sulfate, dextran sulfate and hyaluronic acid [0072-0073].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the immunostimulants (GM-CSF) of Bell within the coated solid compositions of Saito. One would do so with a reasonable expectation of success because Bell teaches bone precursor compositions that contain in addition to therapeutic agents, growth factors, specifically colony stimulating factors, such as GM-CSF, that are advantageous in providing regulation of differentiation and development. The expected result would be an improved composition for treating diseases and conditions of bone.

* * * * *

Claims 1-6, 8, 11, 12, 19, 22, 24-26, 28-29, 32-34 and 36-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petersen *et al.* (hereinafter "Petersen") (U.S. Pat. Appln. Publn. No. 2002/0071827 A1) in view of Saito *et al.* (hereinafter "Saito") (U.S. Patent No. 6,344,209) and further in view of Bell *et al.* (hereinafter "Bell") (U.S. Pat. Appln. Publn. No. 2002/0055143 A1).

Petersen ('827) teaches a bone graft substitute composition that may include a mixture comprising calcium sulfate hemihydrate, plasticizing substances - cellulose derivatives such as hydroxypropylmethyl cellulose, bioactive agents such as hyaluronic acid, growth factors, bone marrow, etc. and additives such as antitumor agents. See ¶s [0014]-[0020]; [0041]-[0045].

The bone graft substitute composition can be mixed into a paste and then loaded into a syringe and ejected for an extended period of time [0016].

Petersen teaches inclusion of antitumor agents. Petersen does not teach cisplatin.

Saito ('209) teaches an apatite-coated solid composition containing a biodegradable polymer, an apatite-coated solid composition containing a biodegradable polymer and a medicinal substance having sustained release properties and a method for producing the solid composition (see column 1, lines 6-10); (col. 2, line 39 – col. 3, line 37) and Abstract.

Suitable medicinal substances disclosed are anti–tumor agents including antineoplastic agents such as cisplatin (col. 6, line 65 – col. 7, line 3). The medicinal substance is employed before molding with the aid of suitable excipients such as calcium sulfate hemihydrate (col. 15, lines 21-33).

The apatite-coated solid composition can be used to treat and repair bone tissue after surgery for lung cancer, breast cancer, etc. (col. 20, lines 43-58).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the antitumor/antineoplastic agents (cisplatin) of Saito within the bone substitute compositions of Petersen. One would do so with a reasonable expectation of success because Saito teaches an apatite-coated solid composition containing biodegradable polymers in combination with medicinal substances, such as the antineoplastic agent - cisplatin, which is used for the effective combat and treatment of various types of cancers (i.e., breast cancer). The expected result would be an improved and enhanced chemotherapeutic composition for the treatment of cancers.

The teachings of Petersen are discussed above. Petersen teaches growth factors [¶ 0050]. Petersen does not teach an immunostimulant such as GM-CSF.

Bell ('143) teaches bone precursor compositions suitable for injection, which contain calcium sulfate hemihydrate, therapeutic agents and colony stimulating factors (CSF), such as GM-CSF. The colony stimulating factors (growth factors) are beneficial in the regulation of differentiation and development. See ¶s [0009-0010]; [0056]; [0069]. Additional agents disclosed include chondroitin sulfate, dextran sulfate and hyaluronic acid [0072-0073].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the immunostimulants (GM-CSF) of Bell within the bone graft substitute compositions of Petersen. One would do so with a reasonable expectation of success

because Bell teaches bone precursor compositions that contain in addition to therapeutic agents, growth factors, specifically colony stimulating factors, such as GM-CSF, that are advantageous in providing regulation of differentiation and development. The expected result would be an improved composition for treating diseases and conditions of bone.

* * * * *

Response to Arguments

Applicant's arguments filed 03/13/09 have been fully considered and were found to be partially persuasive.

- **Rejection under 35 U.S.C. §103(a) over Saito (USPN 6,344,209) & Bell (US 2002/0055143A1):**

Applicant argued, "Saito relates to an apatite-coated solid composition. Preformed apatite particles and a medicinal are simply mixed with a polyester. It does not relate to a composition where the active agents are "dispersed throughout *a matrix"* and which is "the *hydration reaction product of an aqueous mixture comprised of: an inorganic compound capable of undergoing hydration and/or crystallization,* an antineoplastic agent, *an immunostimulant,* and at least one of: a matrix polymer, a complexing agent, and a conditioning agent (emphasis added)."

Bell relates to a bone precursor composition comprising a calcium cement which is suitable for injection, wherein said calcium cement includes monobasic calcium phosphate monohydrate and beta-tricalcium phosphate. However as noted above, the "coated solid composition" of Saito is very different from the matrix composition of the subject invention

and combining Saito and Bell would in no way arrive at the composition of the subject invention. There is no suggestion in these references of including both an antineoplastic agent (e.g. cisplatin) and an immunostimulant (e.g.GM-CSF)."

Applicant's arguments have been fully considered but they are not persuasive. Applicant's arguments are directed to the manner by which their composition is formed, such as by the antineoplastic and immunostimulant being dispersed throughout a matrix and being the hydration reaction product of an aqueous mixture of: an inorganic compound (capable of undergoing hydration and/or crystallization), an antineoplastic agent, an immunostimulant, and at least one of: a matrix polymer, a complexing agent, and a conditioning agent. It is the position of the Examiner that the teachings of the prior art are sufficient to render the instant claims *prima facie* obvious. The prior art teaches a controlled release composition comprising the same components as claimed by Applicant. Namely, the prior art recognizes and teaches compositions containing a biodegradable polymer (i.e., hyaluronates); or an apatite-coated solid composition containing a biodegradable polymer and a medicinal substance (i.e., anti–tumor agents such as antineoplastics), whereby the composition has sustained release properties. A method for producing the solid composition is also disclosed (see column 1, lines 6-10); (col. 2, line 39 – col. 3, line 37). The composition further teaches matrix polymers such as the polysaccharide - hyaluronic acid (col. 20, lines 9-32) and inorganic compounds capable of undergoing hydration and/or crystallization, such as calcium sulfate hemihydrate (col. 15, lines 21-33). Thus, the process by which the instant composition is formed does not impart patentability to the claims. The art is clearly suggestive of a controlled release composition formed of the same elements as desired by Applicant. "[E]ven though product-by-process claims are limited by and defined by

the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it is noted that while Saito does not teach an immunostimulant such as GM-CSF, the secondary reference of Bell remedies this deficiency of Saito. Bell teaches that it is well known to one of ordinary skill in the art to employ therapeutic agents such as the immunostimulant - GM-CSF in bone compositions. Note that Bell also teaches inorganic compounds capable of undergoing hydration and/or crystallization, such as calcium sulfate hemihydrate. Additional agents disclosed by Bell include matrix polymer such as chondroitin sulfate, dextran sulfate and hyaluronic acid [0072-0073]. Thus, both references are drawn to the same field of use (bone forming/precursor compositions). One would incorporate the immunostimulant - GM-CSF, as taught by Bell within the bone compositions of Saito, since the use of these (GM-CSF) therapeutic agents in bone compositions is routine to one skilled in the

art. Absent a showing of evidence to the contrary, the formulations of the prior art would achieve the same beneficial results as instantly sought by Applicant.

- **Rejection under 35 U.S.C. §103(a) over Petersen (US 2002/0071827) in view of Saito (USPN 6,344,209) & Bell (US 2002/0055143A1):**

Applicant argued, "The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the antitumor/antineoplastic agents (cisplatin) of Saito or the immunostimulants of (GM-CSF) of Bell within the bone substitute compositions of Petersen. However as noted above, the "coated solid composition" of Saito is very different from the matrix composition of the subject invention and combining Saito and Bell would in no way arrive at the composition of the subject invention. Again, there is no suggestion in these references of including both an antineoplastic agent (e.g. cisplatin) and an immunostimulant (e.g. GM-CSF)."

Applicant's arguments were not rendered persuasive. As delineated above, Applicant's arguments are directed to the manner by which their composition is formed, such as by the antineoplastic and immunostimulant being dispersed throughout a matrix and the composition being formed due to a hydration reaction based on an aqueous mixture of: an inorganic compound (capable of undergoing hydration and/or crystallization), an antineoplastic agent, an immunostimulant, and at least one of: a matrix polymer, a complexing agent, and a conditioning agent. It is the position of the Examiner that the teachings of the prior art are sufficient to render the instant claims *prima facie* obvious. The prior art, in combination, teaches a controlled release composition comprising the same components as claimed by Applicant. Thus, the

process by which the instant composition is formed (i.e., hydration reaction) does not impart and accord patentability to the claims. The claims merely require a controlled release composition formed of drug (immunostimulant, antineoplastic); inorganic compound (calcium sulfate hemihydrate) and matrix polymer (hyaluronic acid). The art is clearly suggestive of a controlled release composition formed of these same elements as desired by Applicant. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). Furthermore, "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Absent a showing of evidence to the contrary, the formulations of the prior art would achieve the same beneficial results as instantly sought by Applicant; the process by which the product is made failing to accord patentable weight to the present claims.

- **Double Patenting:**

Applicant argued, "None of the commonly owned patents cited by the Examiner as the basis of the double patenting rejection relate to a sustained release matrix composition containing BOTH an antineoplastic agent and an immunostimulant. It is this combination that provides an enhanced immune response to cancer cells. Accordingly, the presently claimed invention is not a mere obvious variant to the inventions defined in the cited patents forming the basis of the Examiner's double patenting rejection. Withdrawal of

the double patenting rejection is therefore in order as the presently claimed invention is patentably distinct thereover."

Applicant's arguments have been considered and were rendered persuasive. Accordingly, the double patenting rejections over the (1) 6,869,976 Patent; 6,391,336 Patent; 6,497,901 Patent and copending Application No. 10/838,303 have been withdrawn.

The remaining rejections of record ((35 U.S.C. 103(a)) have been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

hns

June 25, 2009